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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,316	04/26/2001	Evi Kostenis	38005-147	5658

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EXAMINER	
ULM, JOHN D	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 02/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/842,316	KOSTENIS ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *15 and 20-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims 1 to 31 are pending in the instant application. Claims 1, 9 and 16 to 19 have been amended and claim 32 has been canceled as requested by Applicant in Paper Number 19, filed 02 June of 2003.

2) Claims 15 and 20 to 31 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 11.

3) Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4) The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5) Claims 1 to 4, 8, 10 to 14 and 16 to 19 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for those reasons of record in section 5 of Paper Number 16. Applicant has traversed this rejection on the premise that undue experimentation would not be required to predictably alter the amino acid sequence presented in SEQ ID NO:2 because Applicant has provided "the basic structural templates for comparison (SEQ ID No:2 and SEQ ID No:2) and methods for assaying molecules with EDGE8 activity" as well as "methods for mutatoing the recited sequences".

. Applicant appears to have taken the position that 35 U.S.C. 112, first paragraph, permits an artisan to present claims of essentially limitless breadth so long

as the specification provides one with the ability to test any particular embodiment which is encompassed by the material limitations of a claim and thereby distinguish between those embodiments which meet the functional limitations from those embodiments which don't. This argument is not entirely without merit. However, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. Applicant's "make and test" position is inconsistent with the decisions in *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) which was cited as the judicial basis for the instant rejection in the previous office action, *Amgen v. Chugai Pharmaceuticals Co. Ltd.*, 13 USPQ2d, 1737 (1990), and *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988). *In re Wands* stated that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors were addressed in the initial rejection. As stated therein, claim 1 encompasses an isolated polynucleotide encoding an amino acid sequence which can deviate from SEQ ID NO:2 by as many as 120 residues out of 399. The current claims encompass nucleic acids encoding non-naturally occurring proteins having an amino acid sequence which deviates from the single naturally occurring amino acid sequence disclosed in the instant specification by as many as 120 amino acid residues. These claims encompass

over 20^{120} material embodiments, none of which contain the only functional embodiment described in the instant specification. Breadth alone is not the issue, however. As stated in section 7 of Paper Number 16, *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Having established the breadth of the claims, *Wands* now requires that one consider the number of working examples presented in the instant specification. It is noted that there in not a single example in the instant specification, working or prophetic, of a functional "EDG8" protein whose amino acid sequence deviates from nature by **even a single amino acid residue**. Since there are **no** working examples, then one must consider the guidance provided by the instant specification and the prior art of record. The instant specification provides absolutely no guidance as to which amino acid residues in

SEQ ID NO:2 of the instant application are essential for the functional and structural integrity of an "EDG8" protein and which residues are either substitutable or expendable. Further, there is no functionally and structurally analogous protein which has been identified in the prior art for which this information is known and could be applied to SEQID NO:2 by analogy. In conclusion, the instant claim encompasses nucleic acids encoding a vast, almost limitless, number of function "EDG8" proteins having non-naturally occurring amino acid sequences and yet the instant specification provides no working examples and no guidance that would permit and artisan to practice the invention commensurate with the scope of the instant claims.

Applicant's argument is based upon a premise that the standard under 35 U.S.C. 112, first paragraph, is that of mutating a subject protein and testing to see if it retains the desired biological activity is a position that has been routinely dismissed by the courts, as shown by those decisions cited above.

Further, *In re Wands* determined that the repetition of work which was disclosed in a patent application as producing a composition containing an antibody, which is a naturally occurring compound, did not constitute undue experimentation even if the antibody produced thereby was not identical to those that were disclosed in that application. The instant claims are not limited to naturally occurring compounds and the instant specification does not provide a description of a repeatable process of producing an isolated nucleic acid encoding an "EDG8" protein whose amino acid deviates from the single disclosed, naturally occurring sequence by as much as 33%. To practice the instant invention in a manner consistent with the breadth of the claims would not require

just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues in the amino acid sequence of SEQ ID NO:2 which are required for the functional and structural integrity of that protein. It is this additional characterization of that single disclosed, naturally occurring, protein that is required in order to obtain the functional and structural data needed to permit one to produce an isolated nucleic acid encoding an "EDGE*" protein which meets both the structural and functional requirements of the instant claims that constitutes undue experimentation.

With regard to the propriety of specifically considering the decisions of *In re Fisher*, *Amgen Inc. v. Chugai*, and *In re Wands* to the exclusion of other judicial decisions in determining the patentability of the instant claims, Applicant is encouraged to review the discussion of 35 U.S.C. 112, first paragraph in the CAFC decision, *Genentech, Inc. v. Novo Nordisk*, 42 USPQ2d, 100 (CAFC 1997), in which these three decisions were considered as the controlling precedents in determining enablement issues where protein and recombinant DNA issues are concerned. These decisions have been relied upon in the instant rejection and by the court because they show that the judicial interpretation of the first paragraph of 35 U.S.C. 112 requires that the breadth of claims must be based upon the predictability of the claimed subject matter and not on some standard of trial and error. To argue that one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound. Unless one has a **reasonable expectation** that any one material

embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are **more likely to work that not** without actually making and testing them then the instant application does not support the breadth of the claims. In the instant case it is highly improbable that any protein having 67% amino acid sequence identity to the disclosed protein will more likely than not perform in the manner disclosed and the instant specification does not provide the guidance needed to predictably alter that sequence with any reasonable expectation that the resulting protein will function as an ":EDG8" protein.

6) Claims 1 to 14 and 16 to 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6.1) These claims are vague and indefinite in so far as they employ the term "EDG8" as a limitation for those reasons of record as applied to claims 18 and 32 in section 11.2 of Paper Number 12. As stated therein, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of "EDG8" an artisan can not determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation. As stated ion the previous rejection, "if it is Applicant's intention to define the limitation "EDG8 biological activity" in terms of a specific activity, then it is this defining activity which should be recited in the claims **in place of** that limitation".

6.2) These claims are also vague and indefinite because the metes and bounds of the limitation "related lysophospholipid mediators" are undeterminable.

7) Claims 1 to 8, 10 to 14 and 16 to 19 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by each of the Glucksmann et al. (WO 00/11166 A1, 02 Mar. 2000) and Behan et al. (WO 00/22131, 20 Apr. 2000) patent publications for those reasons of record in section 13 of Paper Number 12. As stated therein, the amino acid sequence presented in SEQ ID NO:2 of the instant application appears to be identical to the amino acid sequence presented in Figures 1A and 1B of Glucksmann et al. and amino acid residues 104 to 500 in SEQ ID NO:32 of Behan et al. Applicant's argument that neither of these references describe a nucleic acid encoding a function fragment of the proteins described therein is irrelavent to the rejected claims because a claim is anticipated by any single prior art embodiment encompassed thereby. The instant claims are not limited to nucleic acids encoding functional fragments of SEQ ID NO:2 and Applicant has failed to identify that limitation in the instant claims which excludes the nucleic acids described in these references.

8) Applicant's arguments filed 26 November of 2003 have been fully considered but they are not persuasive for those reasons given above.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN ULM
PRIMARY EXAMINER
GROUP 1600